CHAPTER 13

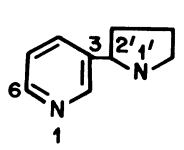
Botanical Insecticides

13.1 Nicotine

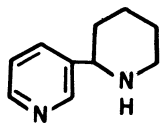
As early as 1690 water extracts of tobacco leaves were used to control sucking insects on garden plants (for the history of nicotine see Shepard 1951; for the reviews see Yamamoto 1965; Schmeltz 1971). The usefulness of this preparation was due to its content of the nicotine alkaloid which is present in tobacco leaves. In addition to nicotine, two other closely related compounds, i.e., nornicotine and anabasine, also have some insecticidal activity (Fig. 13.1). These compounds act as nerve poisons in both insects and mammals, but there is a great deal of variation in susceptibility among different species. Nicotine is obtained from the plants *Nicotiana tabacum* and *Nicotiana rustica* to the extent of 2–8%, but it also occurs in other plants. Nornicotine predominates in *Nicotiana sylvestris* and anabasine is extracted mainly from *Anabasis aphylla.*

13.1.1 Physical and Chemical Properties

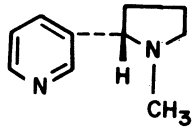
The chemical name of the active nicotine compound is *l*-3-(1-methyl-2-pyrrolidinyl)-pyridine. The commercial name is Black Leaf 40 for the compound containing 40% nicotine sulfate. Free nicotine is a colorless or pale-yellow oily liquid with an acrid burning taste and the odor of pyridine. It is miscible with



R = CH_3, Nicotine
R = H, Nornicotine



Anabasine



Stereostructure of nicotine

Fig. 13.1. Structures of insecticidal tobacco alkaloids. Natural nicotine and anabasine are laevorotatory ($[\alpha]_D^{20}$ = −169; −83.1°, respectively—and the absolute configuration is expressed by D- or S-. Although *l*-nornicotine ($[\alpha]_D^{20}$ = −88.8°) has the same configuration as *l*-nicotine, natural nornicotine occurs as the mixture of *d*- and *l*-forms

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water below 60 °C, and is very soluble in alcohol, chloroform, ether, kerosene, and oils. It is very hygroscopic and turns brown and viscous, with a disagreeable odor, on exposure to air or light. The sulfate form is stable and freely soluble in water and alcohol. Free nicotine, because of its high volatility, is used mainly for fumigation in greenhouses. In agriculture nicotine is used as nicotine sulfate which acts as a stomach poison for leaf-eating insects. Also, the sulfate when sprayed gradually releases free nicotine and is useful to control insects over extended periods. Addition of alkaline compounds such as soap and calcium caseinate liberates the active free nicotine which then acts as a contact insecticide or as a fumigant against soft-bodied insects. Nicotine has largely been replaced by insecticides of greater effectiveness and greater safety to man.

13.1.2 Mode of Action

Nicotine mimics a part of the action of acetylcholine by interacting with the nicotinic acetylcholine receptor, that is, the receptor fails to distinguish between nicotine and acetylcholine. Hence, the effects produced by nicotine across the synapses and neuromuscular functions are called "nicotinic effects" in mammals. In mammals the primary effects of nicotine are at the neuromuscular junctions (voluntary muscles) and other cholinergic junctions such as smooth muscle and glands, whereas in insects the effects are on ganglia of the central nervous system, because the insect neuromuscular junction is not cholinergic. Both acetylcholine and nicotine produce stimulation at low concentrations and blockage at high concentrations. In actual poisoning one observes these two effects in sequence, first stimulation then blockage, so that early twitching and convulsions are followed later by paralysis.

Structure–toxicity studies of many nicotine-like compounds (Yamamoto et al. 1962) showed that essential structural moiety for higher toxicity is the 3-pyridylmethylamino group; the basicity of the nitrogen atom must be high enough to ionize at physiological pHs (pKa preferably 7.4–9.0), and the distance between the two nitrogen atoms should approximate to the distance between the two functional groups of acetylcholine (quaternary nitrogen and carbonyl) (for more details see Chap. 16). Nicotine has no inhibitory effect on cholinesterase activity (Richards and Cutkomp, 1945). However, at higher concentrations the enzyme is inhibited by nicotine and serves as a model of the nicotinic acetylcholine receptor (Yamamoto et al. 1968).

13.1.3 Toxicity to Mammals

For higher animals nicotine is one of the most rapid and toxic poisons known. The smallest single dose fatal to man appears to be about 60 mg and death can occur in 5–30 min. Nicotine is absorbed rapidly from the tongue or eyes, but more slowly from the stomach because of the acidity of the gastric juice. In the free form nicotine is rapidly absorbed through the unbroken skin. As little as 3 ml of 40% free nicotine rubbed on the skin of the abdomen of a cat can rapidly be fatal, whereas much larger amounts of nicotine sulfate have no effect.

Laboratory animals poisoned with nicotine show symptoms of salivation and vomiting, followed by muscular weakness, tremors, hyperexcitability, incoordination, and ultimately, convulsions and, cessation of respiration. The cause of death usually is the result of respiratory paralysis. If respiration is resumed after the convulsions stop, the animal usually survives. The LD_{50} of nicotine sulfate to the rat is oral 83 mg/kg and dermal 285 mg/kg (Gaines 1969). Since nicotine is strictly a nervous system poison interfering with nervous integration both in insects and mammals, it is much less toxic to lower organisms which are devoid of a well developed nervous system.

13.1.4 Toxicity to Insects

Although nicotine is usually classed as a contact insecticide, it probably acts largely as a fumigant even when applied as a dust or spray. One mode of entry of nicotine into the insect is thought to be as a gas passing through the spiracles into the tracheal system. Symptoms of poisoning by nicotine follow the general sequence of excitation, convulsions, paralysis, and death.

13.1.5 Metabolism

Nicotine is the active principle of tobacco smoke and as such its metabolism has been studied extensively in man and animals (Schmeltz 1971; Fig. 13.2). Oxidation occurs on 5'-carbon atoms, 1'-nitrogen atom, and on the N-methyl group of nicotine to form cotinine, nicotine-1'-oxide, and nornicotine, respectively. Methylation on the pyridyl nitrogen atom occurs also to give nicotine isomethonium. Different from animal metabolism, soil bacteria oxidized nicotine on 6-carbon to form 6-hydroxynicotine. In all animals tested the major metabolic product was found to be cotinine, which is further converted to several metabolites, and eventually to 3-pyridylacetic acid. Nornicotine follows a pathway similar to that of nicotine. Insects convert nicotine mainly to cotinine together with several unidentified products. Certain tobacco-feeding insects metabolize nicotine to avoid intoxication, while others (e.g., tobacco hornworm, tobacco budworm, and cabbage looper) do not metabolize nicotine, but efficiently excrete it into feces.

13.1.6 Therapy

Artificial respiration is always lifesaving provided it is given before there is a severe drop in blood pressure (Franke and Thomas, 1933, 1936). If the poison is swallowed give activated charcoal. Vomiting should be induced if the poison itself has not produced vomiting. Poisoning can also be treated with anticonvulsants.

13.2 Rotenone

There are a group of compounds in the roots of *Derris* and other plants of the family *Leguminosae* which are similar to rotenone in chemical structure, such as

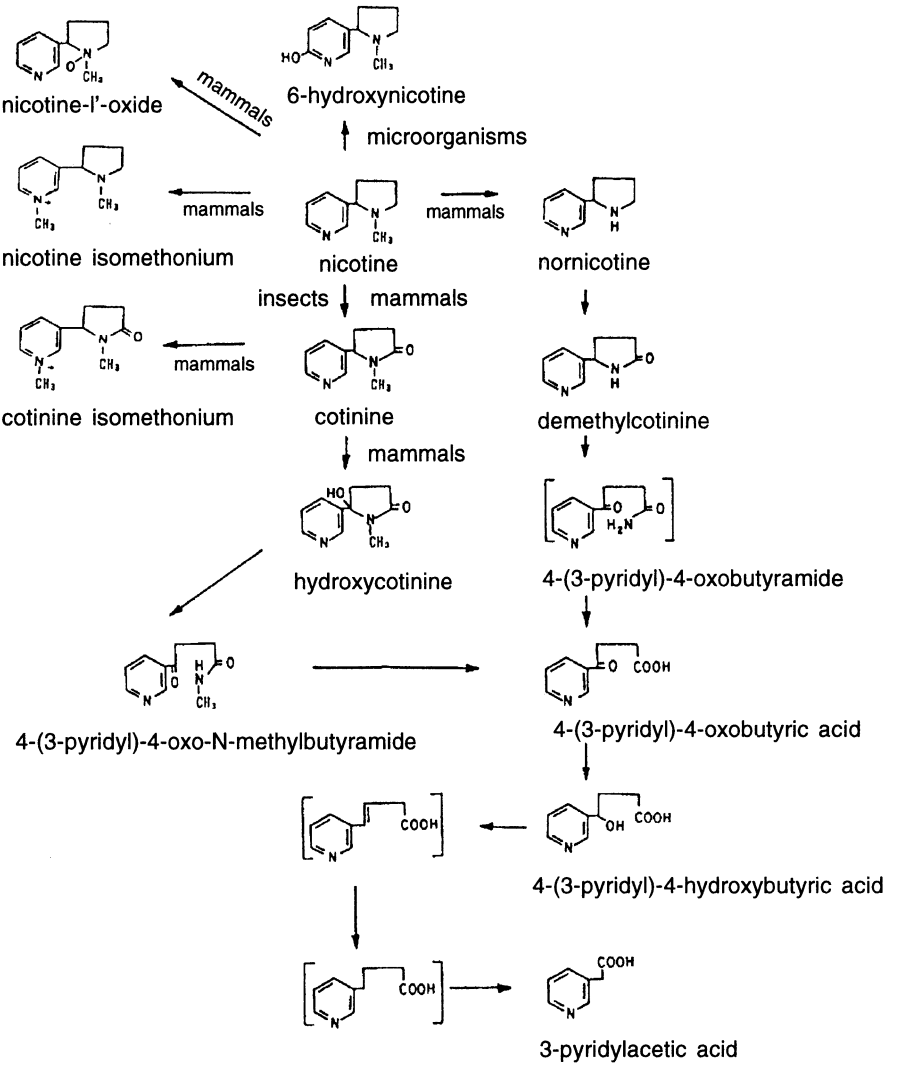


Fig. 13.2. Metabolism of nicotine in mammals, insects, and microorganisms. (Schmeltz 1971)

deguelin, toxicarol, sumatrol, elliptone, malaccol, dalpanol, pachyrrhizone, dolineone, amorphin, munduserone, and erosone, collectively called rotenoids. However, rotenone is the most important compound and insecticidal preparations of it have been used in crop protection since 1848 (for review see Fukami and Nakajima 1971). Rotenone occurs in certain leguminous plants (in as many as 68 species), but mainly in *Derris eliptica* grown chiefly in the Far East and in cube root from *Lonchocarpus* spp. which occur in the Amazon Valley of South America. The long slender roots are dried, ground to a powder, diluted with talc, pyrophyllite, clay, sulfur, or similar nonalkaline diluents, and used as insecticide

dusts containing 0.75–1.5% rotenone. These dusts are commonly used for the control of beetles, aphids, weevils, and many other insect pests of truck crops, and against animal parasites such as fleas, lice, and ticks. Rotenone has been used as a lotion for chiggers, as an emulsion for scabies, and as a spray against cattle grubs and mange of dogs.

For use as liquid formulations the roots are extracted with ether or acetone. Such extractives known as derris and cube resins contain about 30–40% rotenone (see Shepard 1951 for details). Natives throughout the tropics have long used rotenone-containing plants as fish poisons. Rotenone is sometimes applied to lakes and ponds to kill undesirable fish before restocking with more desirable varieties. Derris and other rotenone-containing materials undergo decomposition in light and air. Colorless solutions of rotenone in organic solvents, when exposed to light and air, become yellow, orange, and finally red, due to oxidation.

13.2.1 Mode of Action

It has been determined that the mode of action of rotenone poisoning derives from the ability of rotenone to inhibit respiratory metabolism (Fukami 1956, 1961; Lindahl and Oberg 1961; Yamamoto 1970; Storey 1981). More precisely, rotenone interferes with the electrontransport system between NADH dehydrogenase and coenzyme Q at complex I as piericidin A, causing a severe reduction in oxygen consumption (see Chap. 17). Natural rotenone has *cis* or 6aβ, 12aβ, 5'β (6aS, 12aS, 5'R) configurations and is designated as 5'β-rotenone. Synthetically, 5'α-rotenone (6aα, 12aα, 5'α; the optical antipode of natural rotenone), 5'α-epirotenone (6aβ, 12aβ, 5'α), 5'β-epirotenone (6aα, 12aα, 5'β) (Unai and Yamamoto 1973), and two *trans*-rotenones (6aβ, 12aα, 5'β; 6aα, 12aβ, 5'β) (Begley et al. 1990) are produced. Natural rotenone is the highest in inhibiting mitochondrial respiration followed by *trans* (6aβ, 12aα, 5'β)-rotenone, the latter being epimerized to rotenone with acid; 5'α-epirotenone is less inhibitory and all others are not inhibitory.

13.2.2 Toxicity to Mammals

The mammalian toxicity of rotenone varies greatly with the animal species, method of administration, and type of formulation. The acute oral LD_{50} of crystalline rotenone to the rat is 132 mg/kg, to the guinea pig is 60 mg/kg, and to the rabbit the minimal lethal dose is about 1500 mg/kg (Haag 1931). Poisoning by rotenone in man is rare, but local effects include conjunctivitis, dermatitis, pharyngitis, and rhinitis. On ingestion, rotenone produces gastrointestinal irritation, nausea, and vomiting. The estimated fatal oral dose for a 70-kg man is 100–200 g. Inhalation of the dust is more hazardous and it can cause respiratory stimulation followed by respiratory depression, incoordination, clonic or tonic convulsions, muscle tremors, and death from respiratory failure (Haag 1931). Death is slow following a fatal oral dose and may take 2–10 days or more (Lehman 1951–1952).

13.2.3 Toxicity to Insects

Rotenone is both a contact and a stomach poison to insects. It kills insects slowly but causes them to stop feeding almost immediately. Like all other botanical insecticides its life in the sun is short (1–3 days). It is toxic to many insect species, but the poisoning effect is a slow process. In some cases the mouth parts of insects become paralyzed so that they stop feeding and die of starvation. The poisoning sequence is inactivity, locomotive instability, knockdown, paralysis, and slow death. The cause of death, most likely, is due to respiratory failure.

13.2.4 Metabolism

Initial metabolism of rotenone occurs mainly by oxidation at 8', 6'–7', 12 positions and on the methoxyl group as shown in Fig. 13.3. Combination of these reactions gives many more metabolic products (Fukami et al. 1967; Yamamoto et al., 1971b). All metabolites are less inhibitory to the mitochondrial respiration than rotenone, but 8'-hydroxyrotenone is as toxic as rotenone to mice (i.p. LD_{50} 2.8 and 2.6 mg/kg, respectively).

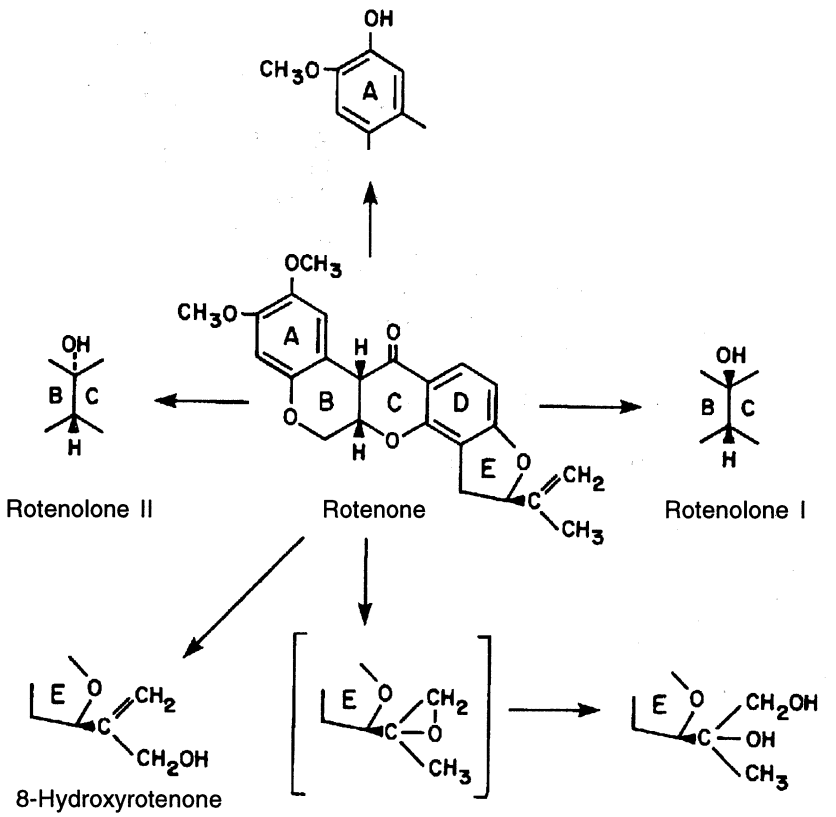


Fig. 13.3. Initial metabolic pathway of rotenone in insects and mammals

13.3 Pyrethrum

13.3.1 Composition and Biological Activity

Pyrethrum is one of the oldest organic insecticides known to man. Even today it is competitive with many of the new generation insecticides for domestic use. This is principally due to its low toxicity to mammals, nonpersistency, and high toxicity to insects coupled with its remarkable effectiveness in causing insect knockdown. The reader may consult excellent available reference books on pyrethrum (Casida 1973; Casida and Quistad 1995a).

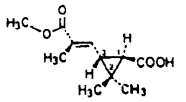
"Pyrethrum" refers to the dried and powdered flower heads of a white-flowered, daisy-like plant belonging to the genus *Chrysanthemum*. The only species of commercial importance is *Chrysanthemum cinerariaefolium*. "Pyrethrins" are all the toxic constituents of the pyrethrum flowers and "pyrethroids" refer to the insecticides based on the pyrethrins as prototypes. "Rethrins" apply to compounds having similar alcohol moiety to pyrethrins. *Chrysanthemum cinerariaefolium* is native to the Dalmatian mountains, Croatia, but Japan was more important as a commercial source before World War II, with, principally Kenya, Uganda, and Rwanda holding the market today. Recently, Australia has become the world's second largest producer.

The pyrethrins are esters formed by a combination of two acids, i.e., chrysanthemic acid and pyrethric acid, with three alcohols (rethrolones), namely pyrethrolone, cinerolone, and jasmolone. The esters of chrysanthemic acid (chrysanthemates) are pyrethrin I, cinerin I, and jasmolin I, and are together known as pyrethrins I. The esters of pyrethric acid (pyrethrates) are pyrethrin II, cinerin II, and jasmolin II, and are together known as pyrethrins II (Fig. 13.4). These six components together account for the toxicity and knockdown properties of pyrethrum extract.

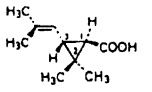
Pyrethrins are generally combined with a synergist in oil sprays and aerosols for use against a wide variety of flying insects. The action of the synergist is to prevent or minimize the breakdown of pyrethrins in the body of the organism. The usual household formulation contains 0.5% pyrethrins and 5% synergist. The most important commercial synergist is piperonyl butoxide. Other synergists, such as extracts of sesame (sesamin and sesamolin), sesamex, propyl isome, and MGK264, have also been used with pyrethrins (see Chap. 15).

Uses. Pyrethrum has been used on many agricultural crops for control of aphids, beetles, mealybugs, leafhoppers, thrips, cabbage worms, loopers, and many others. Formulations of pyrethrins and synergized pyrethrins have been found useful in the control of insect pests associated with households and food commodity storage and processing facilities. They are used extensively as protectants against the ravages of insect pests of stored products, and against insects attacking dried fruits, nuts, and cereal products. Stabilized pyrethrins have proved effective in suppressing certain forest insect defoliators.

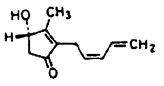
In the field of public health, pyrethrins in combination with the synergist piperonyl butoxide have been used successfully in the control of the brown dog



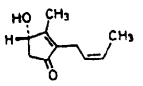
(+) - *trans*-Pyrethric acid



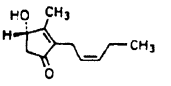
(+) - *trans*-Chrysanthemic acid



(+) - Pyrethrolone

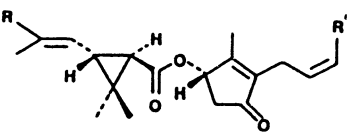


(+) - Cinerolone



(+) - Jasmolone

	R	*R'*
"Pyrethrins I"—esters of chrysanthemic acid (chrysanthemates)		
Pyrethrin I	CH_3	$CH{=}CH_2$
Cinerin I	CH_3	CH_3
Jasmolin I	CH_3	CH_2CH_3



"Pyrethrins II"—esters of pyrethric acid (pyrethrates)		
Pyrethrin II	$CH_3OC(O)$	$CH{=}CH_2$
Cinerin II	$CH_3OC(O)$	CH_3
Jasmolin II	$CH_3OC(O)$	CH_2CH_3

Fig. 13.4. Stereoformula of pyrethrins and constituent acids and alcohols

tick (*Rhipicephalus sanguineus*), for fly control in barns and outdoors, as larvicide for gnat (*Chironomus atrella*) control, as livestock sprays for protection against biting flies, such as stable flies (*Stomoxys calcitrans*), and horn flies (*Haematobia irritans*), for control of ear ticks (*Otobius megnini*), as louse powders, as mosquito repellents, as ultralow volume applications for control of tsetse flies (*Glossina morsitans* and *G. pallidipes*), against tabanid flies, and other insects of public health importance. A development of special significance in medical entomology was the use of pyrethrum aerosols in aircraft making international flights for control of insects, particularly, mosquitoes and other disease vectors, as a quarantine measure.

13.3.2 Mode of Action

Pyrethrins give rapid knockdown action, which is, in many cases, reversible, but could lead to paralysis depending on the dose. The mode of action of pyrethrins is similar to DDT, if not identical, in both insects and mammals. The depolarizing after-potential of a single spike is increased by the application of allethrin (a close analog of pyrethrins) to the giant axon of *Periplaneta americana*, leading

to repetitive discharges and, at higher concentrations, conduction block. Knockdown may be caused by hyperexcitation of the nerve, and nerve block is responsible for paralysis. Pyrethrins, synthetic pyrethroids, and DDT are the only insecticides that possess a clear negative temperature coefficient of the insecticidal action. A housefly strain that is resistant to knockdown by DDT shows cross-resistance to pyrethrum. The gene responsible for kdr selectivity confers resistance to the entire category of both DDT and pyrethroid compounds. Unlike DDT there is a critical temperature below which no repetitive discharges are elicited (see Chap. 14 for further comments).

13.3.3 Toxicity to Insects

Pyrethrum is the insecticide well known for its rapid knockdown action causing temporary paralysis of the insect. The paralytic effect is, in many cases, reversible. This is especially evident in houseflies exposed to pyrethrins. Only minute amounts of the toxicant are needed to produce knockdown, but much larger amounts are required for producing mortality of the flies.

The symptoms of poisoning follow the typical pattern of nerve poisoning, that is, excitation, convulsions, paralysis, and death. The rapidity of action of pyrethrins upon contact with an insect is shown by the excitement with which cockroaches, affected by sublethal quantities of pyrethrum spray, emerge from their hiding places and run about frantically ("flushing effect"). Because they paralyze the insects so rapidly, the pyrethrins could reduce the annoyance from mosquito bites and reduce the opportunity for disease transmission by mosquitoes entering treated dwellings. In the case of DDT residues, the mosquitoes are able to bite before succumbing to the insecticide.

Pyrethrum does not have appreciable effect as a stomach poison and it contains no volatile agent of value as a fumigant, although pyrethrum smokes, produced by burning pyrethrum coils, have for many years been used against flies and mosquitoes. More recently, pyrethrum has been replaced by bioallethrin (a synthetic pyrethroid) for use in smoke coils and other forms of smoke generators.

13.3.4 Toxicity to Mammals

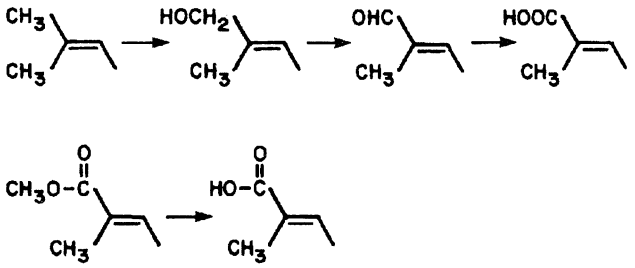
The pyrethrins have an acute oral LD_{50} to rats variously reported, 200–400 mg/kg probably being the range for the less pure preparations, and 400–1500 mg/kg for the more purified preparations (Barthel 1973). The acute toxic effects to laboratory animals proceed from excitation to convulsions to paralysis including muscular fibrillation. Death is caused by respiratory failure. In contrast with human experience, animal tests failed to show the sensitizing effect of pyrethrins.

Despite the long period of pyrethrum use in pest control, only a few documented cases of human poisoning have been reported (Casida, 1973; Hayes, 1982). The pyrethrins show little evidence of causing chronic poisoning; however, they cause some inhalation problems because of impurities in the formulations, resulting in asthma-like symptoms. Dermal toxicity of pyrethrins is negligible because they are poorly absorbed from the skin. The dermal LD_{50} ranges from 1350 to 5000 mg/kg. Many humans have had skin problems (dermatitis) from exposure

to pyrethrins. This dermatitis is an allergic reaction (which may be associated with ragweed sensitivity) and disappears rapidly on removal from exposure. The dermatitis is caused by impurities in the extracts from the flowers which are not present in the current commercial preparations of pyrethrins. Pyrethrins do not pose a hazard of acute toxicity to humans. From the toxicity data available, there is no evidence that pyrethrins are carcinogenic, mutagenic, or teratogenic in test animals or, by extrapolation, in man, although the carcinogenic potential of pyrethrins has not been satisfactorily investigated by modern-day standards. Recent studies on typical manufacturing use extract (a.i. 57.6%) show 2.37 g/kg for males and 1.03 g/kg for females (Schoenig 1995). It can be said that pyrethrum extract has a low order of acute toxicity and very little potential to cause eye or skin irritation and skin sensitization. It is not a teratogen or a reproductive toxin and has minimal potential to induce tumors in the mammalian system, with little or no relevance to human health.

13.3.5 Metabolism

For many years it was considered that the major detoxification mechanism of pyrethrins in insects involved hydrolysis of the ester linkage, splitting the molecule into the acid and alcohol moieties. Later studies demonstrated that a nonhydrolytic mechanism was responsible for the metabolism of pyrethrins and related compounds in insects and mammals. Methylenedioxyphenyl type synergists are known to inhibit oxidative metabolism, by which they increased toxicity. The toxicity of allethrin to houseflies is enhanced by synergists. The major metabolic pathway involves oxidation by the mixed function oxidase system of the *trans*-methyl of the isobutenyl group to the hydroxymethyl metabolite. This initial oxidation step is sensitive to inhibition by the synergists. This metabolite is then conjugated and excreted, or is further oxidized to the aldehyde and then to the acid form (Yamamoto and Casida 1966; Yamamoto et al. 1969).



The terminal methoxycarbonyl of pyrethric acid moiety of pyrethrin II is hydrolyzed. However, oxidation of the alcohol moiety is also important in limiting the toxicity of pyrethrins I and II. The nature of the modification can be inferred from the result of pyrethrin I metabolism in mammals. In insects the initial stage of detoxication involves oxidation independently either on the acid or the alcohol moiety of pyrethrin I, but only on the acid moiety of allethrin, and either methoxycarbonyl cleavage of the acid moiety or oxidation of the alcohol moiety occurs with pyrethrin II, as shown in Fig. 13.5.

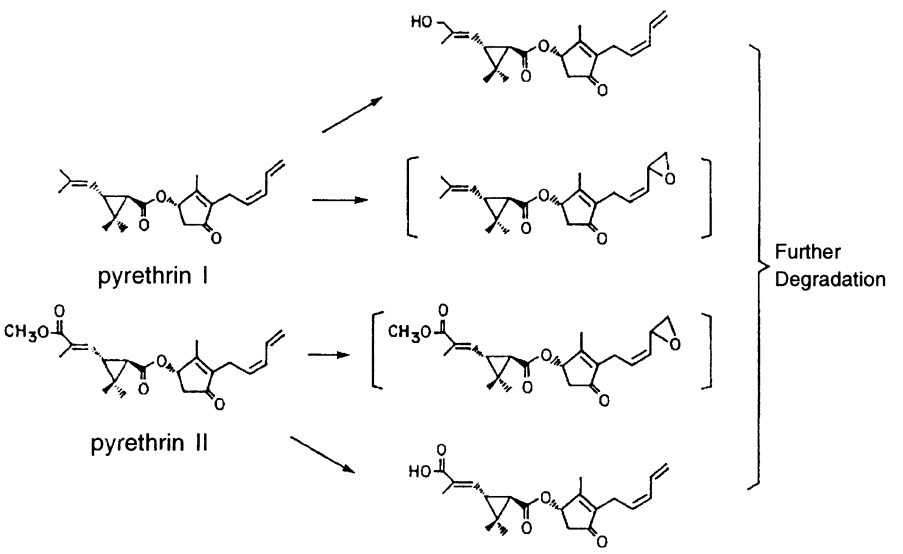


Fig. 13.5. Metabolism of pyrethrin I and pyrethrin II in insects. (Yamamoto 1973)

The scheme explains the facts that pyrethrin I and cinerin I are equal in toxicity to insects when synergized (without synergists cinerin I is inferior to pyrethrin I); pyrethrin II and cinerin II, when synergized, become equal in toxicity, but to a degree around half to one-third of the corresponding chrysanthemates; allethrin is not so synergized as compared with pyrethrins (Yamamoto 1973).

Pathways leading to the urinary metabolites in mammals are shown in Fig. 13.6 (Casida et al. 1971; Elliott et al. 1972).

13.3.6 Advantages and Disadvantages

The disadvantages of pyrethrum are few indeed. Pyrethrum is not a persistent chemical. It is destroyed by light and air and is biodegradable. This is a favorable point on the one hand, but, on the other hand, pyrethrum can only be used as a contact insecticide with little or no residual activity. The allergic responses in man seem to be of less concern when the purified preparations are used. Pyrethrum is toxic to fish and fish food (aquatic insects and crustaceans); however, the low insecticidal concentrations used in spraying operations appear to have a minimal direct impact on fish populations in an aquatic ecosystem (Pillmore 1973). Pyrethrum is also toxic to bees under laboratory testing.

Without doubt, the benefits of pyrethrum certainly outweigh its disadvantages. It is one of the oldest insecticides which has been tried for many years. Pyrethrum controls certain insects as effectively as and more safely than many of the currently used synthetic insecticides. There is no evidence of harm to humans, domestic animals, or wildlife when used as directed. From the toxicity data available, there is no evidence that pyrethrins are carcinogenic, mutagenic, or teratogenic in test animals or, by extrapolation, in man.

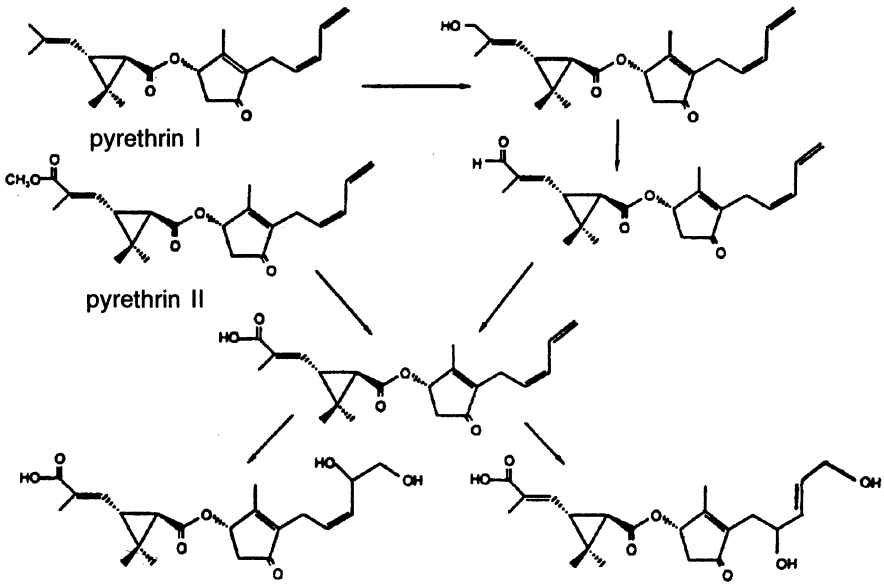


Fig. 13.6. Pathways leading to the urinary metabolites in rats. (Adapted from Casida 1973)

13.4 Neem

Native to India and Burma, the neem tree is a member of the mahogany family, Meliaceae, and is known as margosa tree or Indian lilac, *Azadirachta indica* A. Juss. It is perennial and requires little maintenance for growing. In India an estimated 18 million neem trees are grown, mostly for providing shade to the people. It was introduced to West Africa and other places, and has grown well there. A closely related species, the chinaberry tree or Persian lilac (*Melia azedarach* L.), contains the similar active components as found in *A. indica.*

Its insect control efficacy was first recognized by the withstanding of neem trees from the locust, which swarmed on the tree, but left without feeding. The extracts from seeds and leaves have pest insect control activities. Extraction is easy. The leaves or seeds are merely crushed and steeped in water, alcohol, or other solvents. The extract contains 4 major and perhaps 20 minor active compounds and can be used without further refinement, or the most effective ingredients can be isolated and formulated as commercial products. The affected insect can no longer feed, breed, or metamorphose, and can cause no further damage to crops. Neem oil from seeds is used for many purposes, such as heating, lighting, and lubricating, and in soaps, cosmetics, disinfectants, and others, and neem cake, left after the oil is pressed from the seeds, is effective for soil pests including nematodes (Schmutterer 1990. National Research Council 1992).

13.4.1 Composition and Biological Activity

The main neem chemical is a mixture of three or four related compounds. They belong to tetranortriterpenoid (limonoids) (Fig. 13.7).

1. *Azadirachtin:* the main agent for controlling insects, representing 90% of the effect on most pests; contents are usually 2–4 mg/g kernel. It is a feeding deterrent and growth regulator, repelling and disrupting the growth and reproduction of pests.
2. *Meliantriol:* a feeding inhibitor, causing insects to cease eating in extremely low concentrations.
3. *Salannin:* a powerful feeding inhibitor.
4. *Nimbin and nimbidin:* show antiviral activity.
5. *Others:* minor but also active in one way or another. Deacetylazadirachtin is as active as azadirachtin.

Some neem compounds act as systemics. When exposed to sunlight, neem products degrade and lose their pest-control activities.

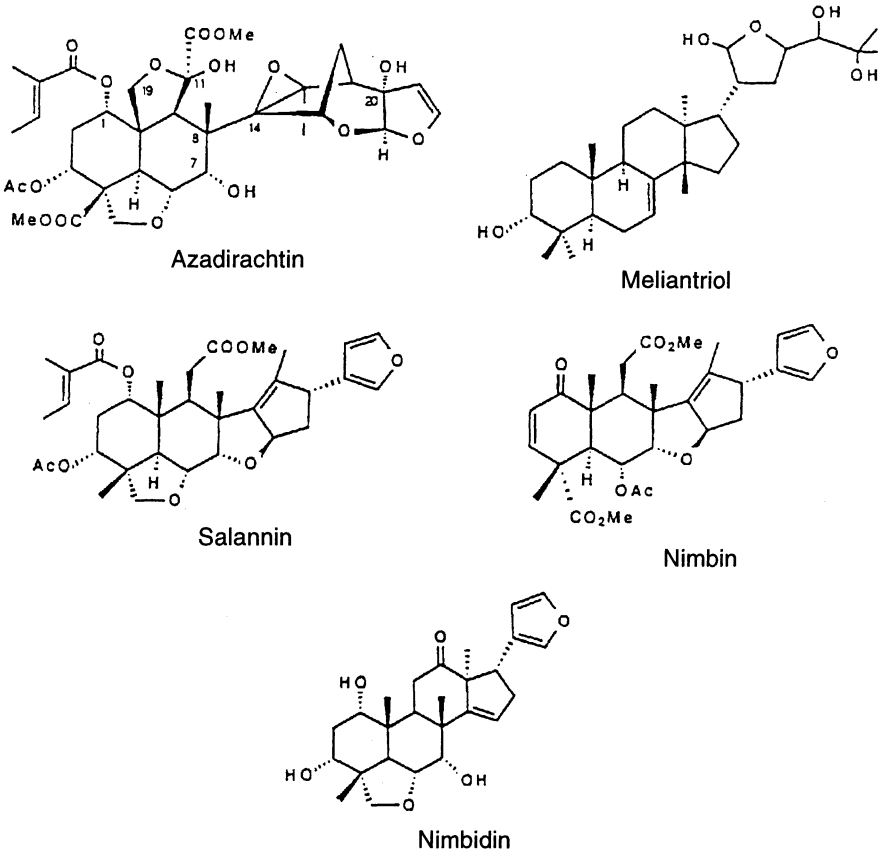


Fig. 13.7. Active neem components

13.4.2 Mode of Action

Azadirachtin is structurally somewhat similar to insect hormones, ecdysones, and seems to be an ecdysone blocker, so that insects will not molt. It also interferes with the function of taste, so that many leaf–eating insects are deterred by plants to which even small amounts of azadirachtin have been applied.

13.4.3 Effects on Insects

Neem preparations show the following effects:

1. Partial reduction or complete inhibition of fecundity and/or sometimes egg hatchability;
2. Reduction of the life span of adults;
3. Oviposition repellence against females;
4. Direct ovicidal effects;
5. Antifeedant effects against larvae, nymphs, or adults;
6. Formation of permanent larvae;
7. Growth regulating effects at molting between larval (or nymphal) instars and especially in the prepupal stage and giving rise to larval–pupal, nymphal–pupal, nymphal–adult, and pupal–adult intermediates, and to crippled adults (Ascher 1993).

13.4.4 Toxicity Problems

Neem has been utilized as a medicinal plant based on general antiseptic activity for generations in India and neem products appear to have little or no toxicity to warm-blooded animals, although no comprehensive toxicology data are available. Neem oil obtained from clean, fungus-free seed kernels showed no oral toxicity in rats at 5000 mg/kg. Neem extracts showed no mutagenicity in the Ames test. However, neem extracts should not be used for internal medicinal purposes. A problem only in the more humid neem-growing areas is that the fruits can carry *Aspergillus flavus*, which produces aflatoxins, the most potent carcinogen. The fungus can contaminate the seeds inside the fruits, and aflatoxins are extracted and concentrated along with pest control ingredients. Neem oil shows toxicity to certain fish species. The seed kernels, whole fruits, or leaves of *Melia azedarach* contain compounds highly toxic to mammals, like meliatoxins. For details about neem refer to Schmutterer (1995).